

CLAIMS

1) "NEW METHOD FOR THE PREPARATION OF 1,5-BIS(4-HYDROXY-3-METOXY-PHENYL)-PENTA-1,4-DIEN-3-ONE AND DERIVATIVES WITH ANTITUMORAL PROPERTIES", characterized by the

5 method for the preparation of 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-one and its derivatives such as compounds with antitumoral activity, responding to the following general formula:

where R1 , R2 , R3 , R4 e R5 can represent hydrogen atoms, prenyl groups, halogen atoms, or acetate or alkyl groups and X one oxygen atom or an ylidemalonitrile group;

10 method for the preparation of 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-ones compound and its derivatives, which are obtained from vanillin and acetone in a 2:1 molar rate in acid medium, in temperatures that changes between 25 and 60 °C, under ultrasonic irradiation conditions in a range from 25 to 40 KHz for a period of 1 to 3 hours further putting the reacted mixture into water / ice until producing the raw product, which

15 dissolves in a solution of sodium hydroxide or potassium hydroxide (between 10-30%) being filtered; the filtrate is treated with hydrochloric acid or sulphuric acid from a concentration between 10-30%, the obtained product being filtered again, finally it is washed with distilled water until obtaining a neutral pH, this operation being repeated until the total purification of the product, not being necessary to perform a new

20 purification of the compound using other procedures such as recrystallization or chromatographic column (the purity was determined by means of the HPLC technique):

Obtained 92% yield of the pure product.

2) "NEW METHOD FOR THE PREPARATION OF 1,5-BIS(4-HYDROXY-3-METOXY-PHENYL)-PENTA-1,4-DIEN-3-ONE AND

25 DERIVATIVES WITH ANTITUMORAL PROPERTIES", according to the claim 1, characterized by the method for the preparation of 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-ones and its derivatives, which are obtained from vanillin and acetone in a 2:1 molar rate in acid medium during 8 days, in temperatures that changes between -10 and 40°C, further putting the reacted mixture into water / ice until producing the raw

30 product, which dissolves in a solution of sodium hydroxide or potassium hydroxide (between 10-30%) being filtered; the filtrate is treated with hydrochloric acid or sulphuric

acid from a concentration between 10-30%, the obtained product being filtered again, finally it is washed with distilled water until obtaining a neutral pH, this operation being repeated until the total purification of the product, not being necessary to perform a new purification of the compound using other procedures such as recrystallization or chromatographic column (the purity was determined by means of the HPLC technique):

Obtained 89% yield of the pure product, melting point of: 155-156 °C.

3) "NEW METHOD FOR THE PREPARATION OF 1,5-BIS(4-HYDROXY-3-METOXY-PHENYL)-PENTA-1,4-DIEN-3-ONE AND DERIVATIVES WITH ANTITUMORAL PROPERTIES", according to the claim 1, characterized by the method for the preparation of 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-ones O and C-prenylated, where the prenyl groups appear linked to oxygen phenol atoms or carbon atoms of the aromatic ring, respectively.

4) "NEW METHOD FOR THE PREPARATION OF 1,5-BIS(4-HYDROXY-3-METOXY-PHENYL)-PENTA-1,4-DIEN-3-ONE AND DERIVATIVES WITH ANTITUMORAL PROPERTIES", according to the claim 1, characterized by the method for the preparation of 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-ones O-prenylated, where equimolecular rate conditions react or in a 2:1 rate of 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-one with prenyl bromide by means of a nucleophilic substitution reaction in presence of a base (K_2CO_3 / DMF) or (NaOMe / MeOH) in a temperature between 20-40 °C during a period of time between 3-8 hours or inert atmosphere reaction (Nitrogen or Argon), further neutralizing the reacted mixture in an acid medium (HCl, or H_2SO_4 or CH_3COOH). The purification of the isolated product can be done using a chromatographic column filled with silica gel and using a mixture of toluene / ethyl acetate or n-Hexane / ethyl acetate as solvents in a appropriate rate.

5) "NEW METHOD FOR THE PREPARATION OF 1,5-BIS(4-HYDROXY-3-METOXY-PHENYL)-PENTA-1,4-DIEN-3-ONE AND DERIVATIVES WITH ANTITUMORAL PROPERTIES", according to the claim 1, characterized by the method for the preparation of 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-ones C-prenylated where 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-ones O-prenylated react in presence of N,N-diethyl-aniline and in inert atmosphere

(Nitrogen or Argon) in a temperature that changes between 210-230 °C for a period of 5-8 hours, followed by the treatment of the reacted mixture by means of adding the necessary quantity of chloroform and consecutive washes with solution of hydrochloric acid and sodium hydroxide, following the drying with sodium sulfate anhydrous, further
5 rotoevaporated; and the formed yellow oil which dissolves in methanol being treated with a small amount of Amberlite IR-120, being stirred for a period of 10 to 60 minutes in a temperature that changes between 20-40 °C, being filtered in room temperature; finally the formed methanolic solution is rotoevaporated, being the reacted product purified by means of a chromatographic column filled with silica gel and using a mixture made of toluene
10 / ethyl acetate or n-Hexane / ethyl acetate as elution solvents in a appropriate rate.

6) "NEW METHOD FOR THE PREPARATION OF 1,5-BIS(4-HYDROXY-3-METOXY-PHENYL)-PENTA-1,4-DIEN-3-ONE AND
DERIVATIVES WITH ANTITUMORAL PROPERTIES", according to the claim 1,
characterized by the method for the preparation of 1,5-bis(4-hydroxy-3-methoxyphenyl)-
15 penta-1,4-dien-3-ones O and C-prenylated starting from vanillin O and C-prenylated or 5-Bromovanillin or 5-Alkylvanillin, reacting with acetone in a 2:1 molar rate in alkaline medium (NaOH / KOH) followed by the corresponding neutralization with hydrochloric acid or sulphuric acid or acetic acid; the purification of the isolated product can be done
20 using a chromatographic column filled with silica gel and using a mixture of toluene / ethyl acetate or n-Hexane / ethyl acetate as solvents in a appropriate rate.

7) "NEW METHOD FOR THE PREPARATION OF 1,5-BIS(4-HYDROXY-3-METOXY-PHENYL)-PENTA-1,4-DIEN-3-ONE AND
DERIVATIVES WITH ANTITUMORAL PROPERTIES", according to the claim 1,
characterized by the method for the preparation of Knoevenagel's derivatives. In a mixture
25 of 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-one and malonitrile or ethyl cyanacetate or methyl cyanacetate in equimolecular rates conditions, adding ammonium acetate, acetic acid and toluene following Cope's variant, heating in reflux for a period of time between 5-16 hours or following Knoevenagel's third variant using piperidine as catalyser. The obtained product is put into water and ice, filtering the precipitate and
30 extracting the aqueous phase with chloroform and washing the chloroform phase with distilled water. Further, the chloroform phase is dried with sodium sulfate anhydrous, filtered and rotoevaporated.